

REMARKS

Reconsideration of the present Application in view of the present Amendments and the following Remarks is respectfully requested. Claims 1-21 are pending in the application. The Examiner deemed the Restriction Requirement set forth in the previous Office Action (Paper No. 8) proper and final. Claims 8, 9, and 11-21 have been withdrawn from further consideration pursuant to 37 C.F.R. 1.142(b), as being directed to a non-elected invention. Therefore, claims 1-7 and 10 are currently under examination. Applicants hereby cancel non-elected claims 8, 9, and 11-21 without prejudice to further prosecution of this subject matter in a related divisional, continuation, or continuation-in-part application. Claims 1-7 and 10 have been amended and new claim 22 has been added to more clearly define the subject matter encompassed by Applicants' invention. Support for the amended and new claims may be found in the specification, for example, at page 7, lines 9-37; page 12, line 39; page 13, lines 1-15; page 13, line 34 through page 14, line 2; and page 14, lines 15-37. No new subject matter has been added.

OBJECTIONS TO THE CLAIMS

The PTO objects to claims 4-7 under 37 C.F.R. § 1.75(c), alleging that the claims are multiple dependent claims that depend upon other multiple dependent claims and thus are in improper form. Consequently, claims 4-7 have not been examined on the merits.

Applicants respectfully submit that claims 4-7 have been hereby amended to place these claims in proper dependent form, in compliance with 37 C.F.R. § 1.75(c). Applicants therefore respectfully request that the objection to claims 4-7 be withdrawn, and submit that these claims can now be examined on the merits.

REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

The PTO rejects claims 1-3 under 35 U.S.C. § 112, second paragraph, for indefiniteness. In particular, the Action asserts that the limitations beginning with the phrase "characterized in that..." recite passive processes that do not reasonably apprise a person skilled in the art of the metes and bounds of the invention. The PTO also alleges that claims 1-3 omit essential elements, in contravention of the requirement for definiteness. Specifically, the

Examiner is unclear with regard to how obtaining a retained cell fraction results in isolation of disseminated tumor cells.

Applicants respectfully traverse these grounds for rejection and submit that in view of the Amendments submitted herewith, claims 1-3 particularly point out and distinctly claim what Applicants regard as their invention. Applicants' invention is directed to a method for isolating disseminated tumor cells from a cell-containing body fluid, comprising passing the cell-containing body fluid or part thereof that comprises a disseminated tumor cell through a screen having a mesh or pore width of about 15 to 30 μm to separate non-cancer cells from disseminated tumor cells, wherein the disseminated tumor cells are retained on the screen, and wherein the body fluid is selected from blood and bone marrow. In certain embodiments, the screen has a mesh or pore width of about 20 μm . In certain other embodiments of the invention, the method comprises separating cellular components from non-cellular components in the body fluid that comprises a disseminated tumor cell to obtain a cell-containing fraction; resuspending the cell-containing fraction in a suspension medium; and passing the resuspended cell-containing fraction through a screen having a mesh or pore width of about 15 to 30 μm to separate non-cancer cells from disseminated tumor cells, wherein the disseminated tumor cells are retained on the screen.

Applicants have amended the claims to remove the phrase "characterized in that [...]" and to define more clearly the steps for isolating disseminated tumor cells from a body fluid. Applicants respectfully submit that the amended claims positively recite the steps of the claimed methods such that a person skilled in the art may reasonably determine the metes and bounds of the present claims. Furthermore, the amended claims clearly point out that disseminated tumor cells are isolated by passing a cell-containing body fluid that comprises such cells, or a resuspended cell-containing fraction that comprises such cells, as recited in the instant claims, through a screen having a mesh or pore width of about 15 to 30 μm , and thereby retaining the disseminated tumor cells on the screen.

Additionally, with regard to "disseminated tumor cells" derived from a body fluid that is blood or bone marrow, Applicants respectfully point out that the specification clearly describes such cells, for example at page 2, lines 15-19 and at page 6, line 38 through page 7, line 7. Blood or bone marrow may therefore contain disseminated tumor cells that have detached

from a primary tumor, and which circulate in these body fluids. This vascular entry through hematologic specialization of disseminated tumor cells that are found in blood and bone marrow is distinct from the shedding of multicellular aggregates from solid tumors, as is found in non-circulating local metastases such as ascitic fluids and effusions. Accordingly, the specification is quite clear regarding how obtaining a retained cell fraction from a body fluid that is blood or bone marrow results in isolation of a disseminated tumor cell.

Applicants therefore submit that the present claims meet the requirements for definiteness under 35 U.S.C. § 112, second paragraph, and respectfully request that the rejection of the claims be withdrawn.

REJECTION UNDER 35 U.S.C. § 102

Claims 1-3 and 10 stand rejected under 35 U.S.C. § 102(b), as allegedly anticipated by Rye et al. (*American Journal of Pathology* 150:99-106 (1997)). Specifically, the Action asserts that Rye et al. teach a method for isolating tumor cells from blood, bone marrow, ascitic or pleural fluids, and from enzyme-digested tissue biopsies, which method allegedly comprises filtering a suspension of cells through a 20-micron nylon microfilament filter to obtain a retained fraction of cells.

Applicants respectfully traverse these grounds for rejection and submit that Rye et al. fail to anticipate the present claims. Applicants' invention is directed to a method for isolating disseminated tumor cells from a cell-containing body fluid, comprising passing the cell-containing body fluid or part thereof that comprises a disseminated tumor cell through a screen having a mesh or pore width of about 15 to 30 μm to separate non-cancer cells from disseminated tumor cells, wherein the disseminated tumor cells are retained on the screen, and wherein the body fluid is selected from blood and bone marrow. In another embodiment, Applicants' invention is directed to a method for isolating disseminated tumor cells from a cell-containing body fluid, comprising separating cellular components from non-cellular components in the body fluid to obtain a cell-containing fraction that comprises a disseminated tumor cell; resuspending the cell-containing fraction in a suspension medium; and passing the resuspended cell-containing fraction through a screen as recited. In certain particular embodiments, the screen has a mesh or pore width of about 20 μm .

Applicants respectfully submit that Rye et al. fail to anticipate each and every limitation of the instant claims and, therefore, cannot be regarded as novelty-destroying. Rye et al. fail to teach or suggest a method for isolating disseminated tumor cells in which a disseminated tumor cell-containing body fluid is passed through a screen to separate non-cancer cells from disseminated tumor cells, wherein the disseminated tumor cells are retained on the screen. Rye et al. also fail to teach or suggest separating cellular components from non-cellular components in the body fluid to obtain a disseminated tumor cell-containing fraction that is resuspended and passed through a screen having a mesh or pore width of about 15 to 30 μm to separate non-cancer cells from disseminated tumor cells. Instead, Rye et al. merely teach that mononuclear cells must first be isolated from blood and then filtered through larger pore, 70- and 40 μm , strainers. Tumor cells are then selected from the cells retained on the strainers by incubating the cells with antibody-conjugated magnetic beads (immunobeads). The immunobeads to which tumor cells have bound may then be separated from cells that do not bind to the immunobeads (*e.g.*, non-tumor cells) by exposing the immunobeads to a magnet. The magnetic immunobead fraction is then filtered through a 20 μm filter. *See* Rye et al., page 101, 1st column. Applicants therefore respectfully submit that Rye et al. do not anticipate the present claims and request that the Examiner withdraw this rejection.

The PTO also rejects claims 1-3 and 10 under 35 U.S.C. § 102(e), asserting lack of novelty. In particular, the Action asserts that U.S. Patent No. 6,265,229-B1 (Fodstad et al.) teaches a method for isolating micrometastatic tumor cells from various bodily fluids, the method comprising filtering a suspension of cells through a porous membrane, preferably a membrane that has 20 micron pores, to obtain a retained fraction of cells.

Applicants respectfully traverse these grounds for rejection and submit that Fodstad et al. fail to anticipate each and every limitation of the present claims. Fodstad et al. fail to teach or suggest a method for isolating disseminated tumor cells in which a disseminated tumor cell-containing *body fluid* is passed through a screen having a mesh or pore width of about 15 to 30 μm to separate non-cancer cells from disseminated tumor cells, wherein the disseminated tumor cells are retained on the screen. Fodstad et al. also fail to teach or suggest a method for isolating disseminated tumor cells in which a disseminated tumor cell-containing body fluid is first subjected to a step to *separate cells from non-cellular material*, followed by

passing the resuspended cellular component through a screen having a mesh or pore width of about 15 to 30 μm that retains the disseminated tumor cells.

By way of contrast, Fodstad et al. merely teach a method for isolating a target cell not by retention on a screen but by specific binding to an insoluble bead or particle. According to the method of Fodstad et al., a target cell is linked to an insoluble support, such as paramagnetic beads or particles, followed by isolation of the insoluble support/target cell as an artificial complex (*see, e.g., Fodstad et al., column 3, lines 14-39*). This artificial preparation comprising the insoluble support/target cell complex may then be further isolated by filtration according to Fodstad et al. (*see, e.g., Fodstad et al., column 8, lines 37-44*). Applicants respectfully submit, however, that this filtration step of Fodstad et al. pertains neither to passing a disseminated tumor cell-containing *body fluid* through a screen, nor to passing a cell-containing fraction *from which non-cellular components have been separated* through a screen, as recited by the instant claims. Instead, Fodstad et al. are concerned with removing unbound beads, non-specifically bound cells and unbound non-target cells from an artificial, heterogeneous suspension that includes non-cellular components, in particular, insoluble supports (beads). Applicants therefore respectfully submit that the teachings of Fodstad et al. fail to meet each limitation of the present invention and thus fail to anticipate the instant claims. Furthermore, and for reasons also given above, the documents cited by the PTO (including those not relied upon by the Action) fail to teach or suggest isolating disseminated tumor cells from a cell-containing body fluid that is blood or bone marrow, according to the presently recited methods.

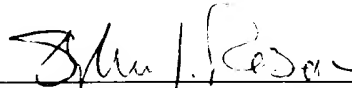
Applicants therefore submit that the subject matter of the present claims is novel, satisfying the requirements of 35 U.S.C. § 102. Applicants respectfully request that the PTO withdraw these rejections.

All claims remaining in the application are now allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

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Enclosures:

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